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Dr Ries speaks for:

- Lilly, Janssen, Pfizer, Forest, Zeneca, Bristol Myers, Abbot,

- States, counties, WAMI, mental health centers, addiction agencies, and others

Severely Mentally Ill Dual Disorder Patients are:

- Under-recognized, with their substance issues under treated, which often leads to
- Revolving Door, High Utilizers (**expensive**)
- Over medicated (**expensive**)
- At high Risk for Suicide (**lethal and expensive**)
- At high Risk for Metabolic Syndromes (**lethal and expensive**)

Dual Disorders Among the Severely Mentally Ill: High Utilizers, Poor Compliance

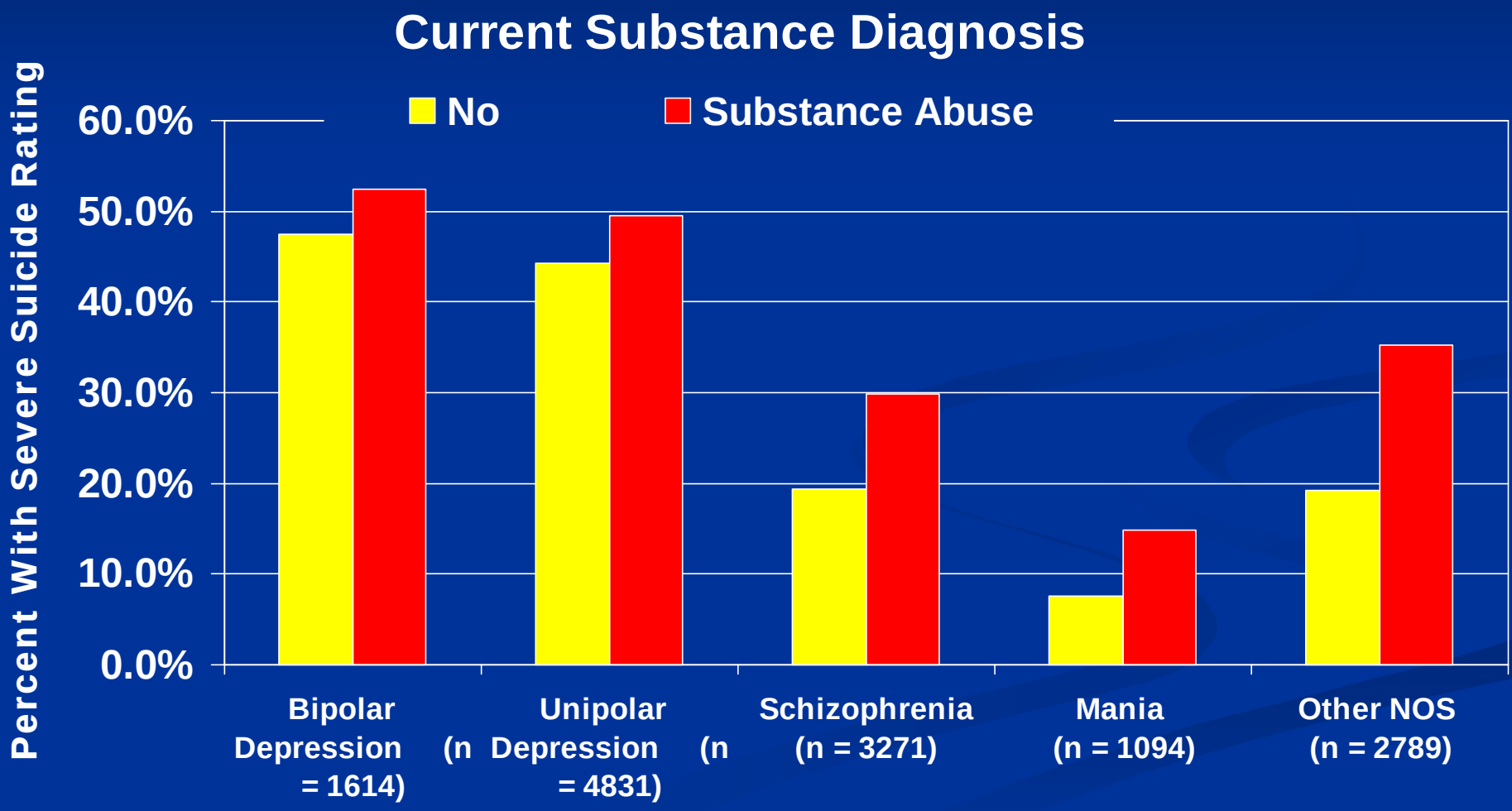
• Hall	’77	Poor out-pt attendance, discontinue Rx
• Alterman	’85	More mood changes, intensive staffing
• Solomon	’86	More noncompliance, arrests
• Safer	’87	Over twice hosp. rate and criminal behav
• Drake	’89	More hostility, noncompliance
• Barbee	’89	More psych symptoms
• Lyons	’89	More noncompliance, ER, jail, rehosp.
• Chen	’92	Worse treatment course

Likelihood of a Suicide Attempt over 5 years (n=20,000)

Risk Factor	Increased Odds Of Attempting Suicide
Cocaine use	62 times more likely
Major Depression	41 times more likely
Alcohol use	8 times more likely
Separation or Divorce	11 times more likely

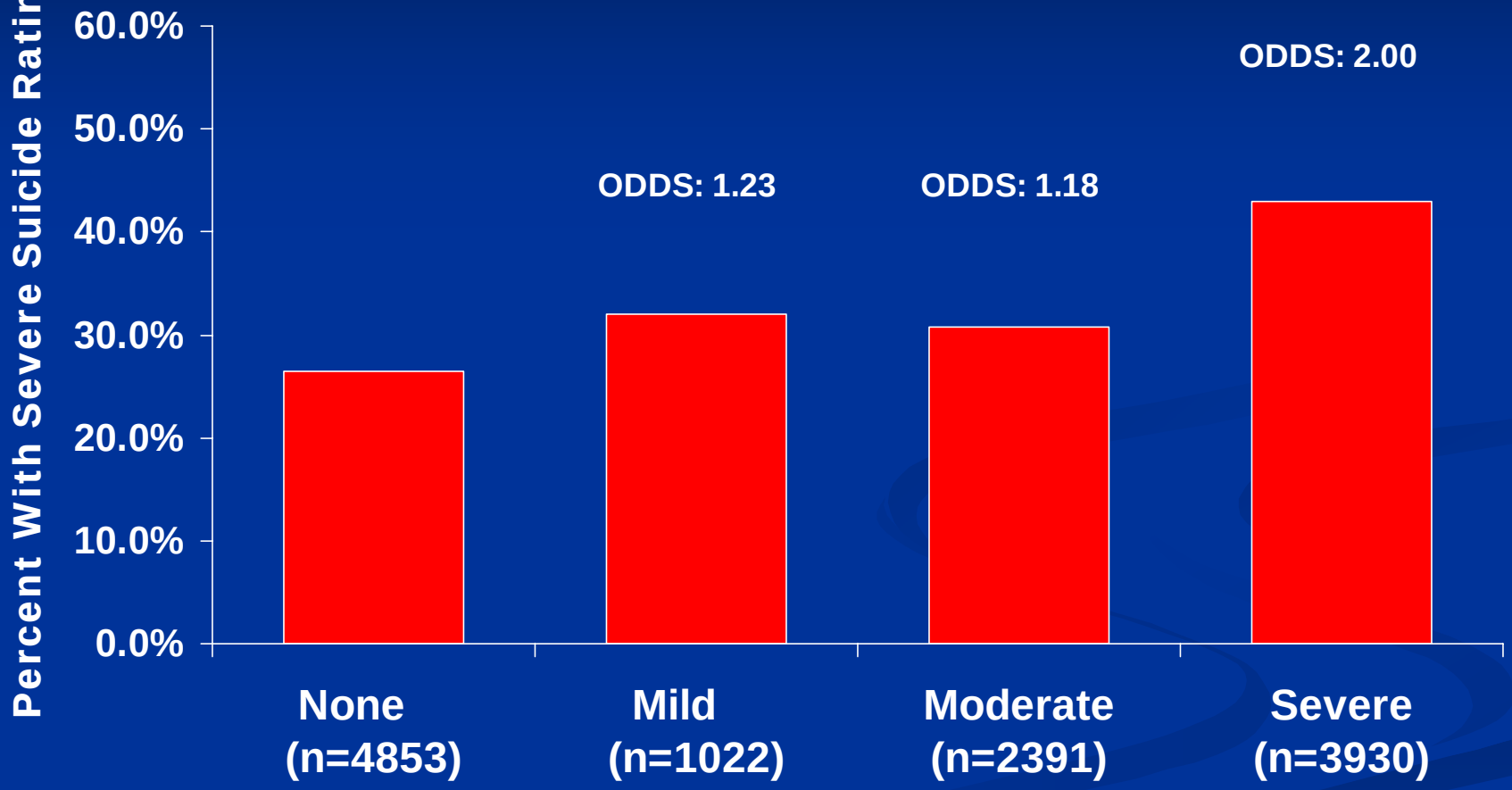
NIMH/NIDA ECA EVALUATION

RELATIONSHIP OF SUICIDE TO PSYCHIATRIC DIAGNOSIS AND SUBSTANCE DEPENDENCE



Ries & Russo, 2003

RELATIONSHIP OF ALCOHOL & DRUG PROBLEMS TO SEVERE SUICIDALITY (n=12,196)



ODDS adjusted for age & gender

Walds = 235.41 p < .001

Ries & Russo, 2003

COD-SMI Program

- Ongoing diagnosis and Rx adjustment
- Bio-psycho-social approach incorporating psychiatric, addiction, and rehabilitation principles and co-trained staff
- Groups: Pre-treatment, Active Rx and Relapse Prevention/support
- Consumer involvement, RECOVERY oriented, AA consistent
- Pre-vocational and vocational incentives as well as payeeship, etc. (carrot and stick)
- What about Medical Health????

Engaging the Chronically Psychotic Patient

- Noncoercive engagement techniques
  - Assistance obtaining food, shelter, and clothing
  - Assistance obtaining entitlements and social services
  - Drop-in centers as entry to treatment
  - Recreational activities
  - Low-stress, non-confrontational approaches
  - Outreach to patient's community
- Coercive engagement techniques
  - Involuntary commitment
  - Mandated medications
  - Representative payee strategies
    - BEST

George is a 32 yo male with :

- Hx consistent with Schizophrenia, chronic paranoid type
- Hx of episodic alcohol and cocaine abuse over the last 10 years
- admitted with severe paranoia, aud halluc, screaming at others downtown

Medication Hx

- Years of Haldol,off and on Lithium and carbamazepine before starting on atypicals about 6 years ago
- Recently was stable on 4 mg Risperidal, but now off meds for weeks
- No medical problems noted in Hx

Inpatient Acute care Treatment Options

- Go back to Haldol
- Go back to 4mg Risperidal
- up the dose to 6 mg Risperidal
- Change to Olanzapine,Seroquel,or Ziprasidone
- Add Depakote, Carbamazepine, and /or Gabapentin
- Use short term BZP's

George stabilizes, is discharged:

- Now on Risperidal and Depakote
- Starts using alc and cocaine in about 2 months and is readmitted in much the same paranoid aggressive condition
- MD changes meds to Ziprasidone and depakote, uses prn BZP's

Hospitalized again, but this time….

- No cocaine,… but used lots of alcohol
- Presentation is depressed and suicidal along with loss of housing, due to drinking
- MD starts remeron 15 mg hs, since agitation and sleeplessness are problems in the hospital, changes to higher dose Olanzapine “since the other meds weren’t working”
- Discharged to a dual dx treatment program

It may not be that the med(s) stopped working, but……

- The patient stopped the med
- The patient stopped the med AND used drugs and/or alcohol…...
- OR lowered the med and used…
- OR used on top of the med….
- Stimulants (cocaine/amphets) are most MSE destructive.

Dual Dx Program

- Ongoing diagnosis and Rx adjustment
- Bio-psycho-social approach incorporating psychiatric, addiction, and rehabilitation principles and co-trained staff
- Groups: pre-treatment, active Rx and Relapse Prevention/support
- Consumer involvement, recovery oriented
- Pre-vocational and vocational incentives as well as payeeship, etc. (carrot and stick)

Medication Snowball Effect

- Substance related Revolving Door admissions (or dcecomps) often lead to additional medications or
- Higher doses or
- Poly-pharmacy
- When in fact with Sobriety, most dual dx patients actually do better than Non dually diagnosed schizophrenics
- Poly-pharmacy…So What?

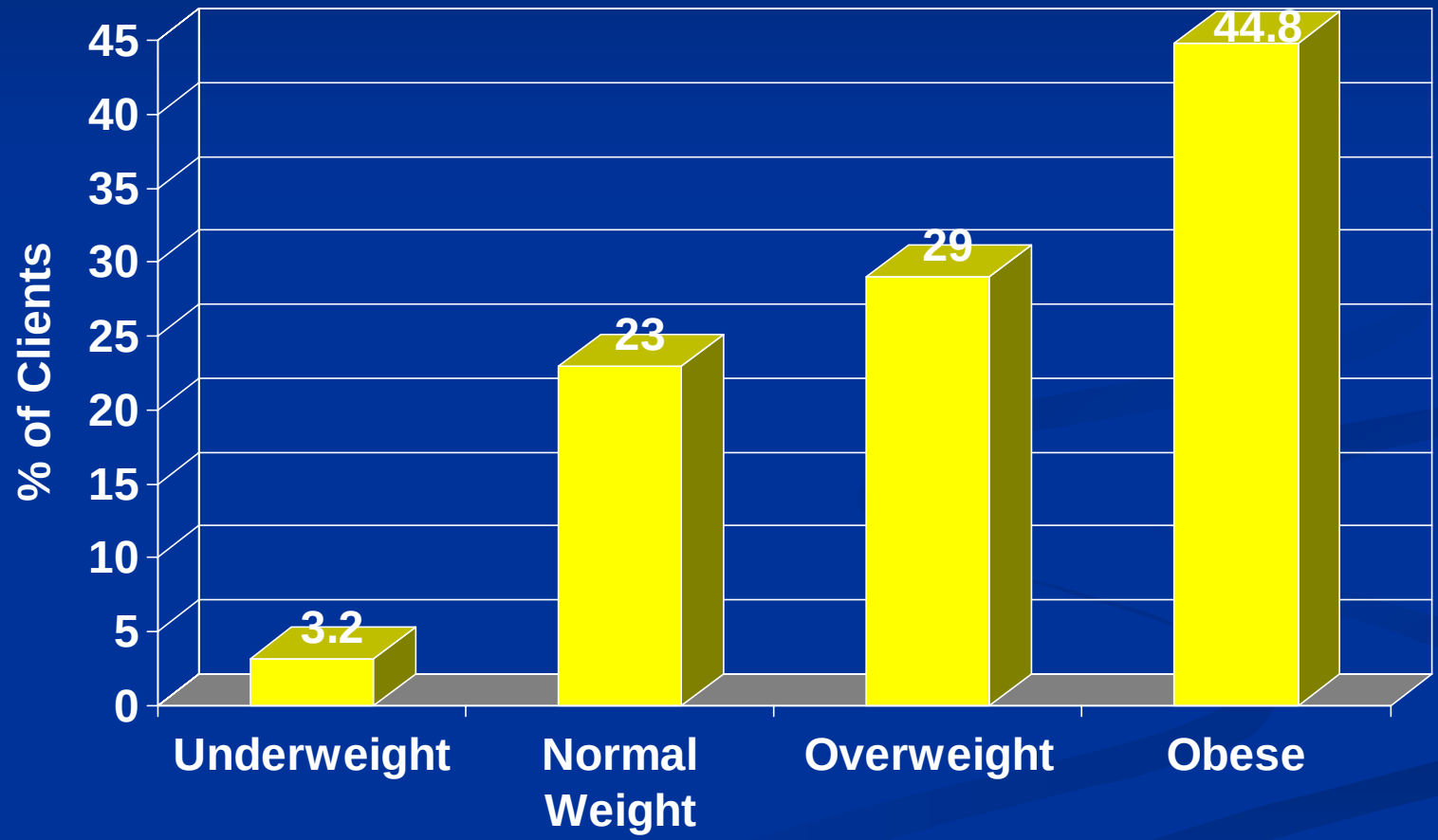
It may not be that the med(s) stopped working, but……

- The patient stopped the med
- The patient stopped the med AND used drugs and/or alcohol…...
- OR lowered the med and used…
- OR used on top of the med….
- OR used all the meds on one day, but none the rest of the week
- Stimulants (cocaine/amphets) are most MSE destructive.

Cause of death in HMHS long term patients

- Cardiovascular……..50%
  - profile average is 49 yo male
- Other medical illnesses and accidents……25%
- Suicide ……17%
- Other ……8%

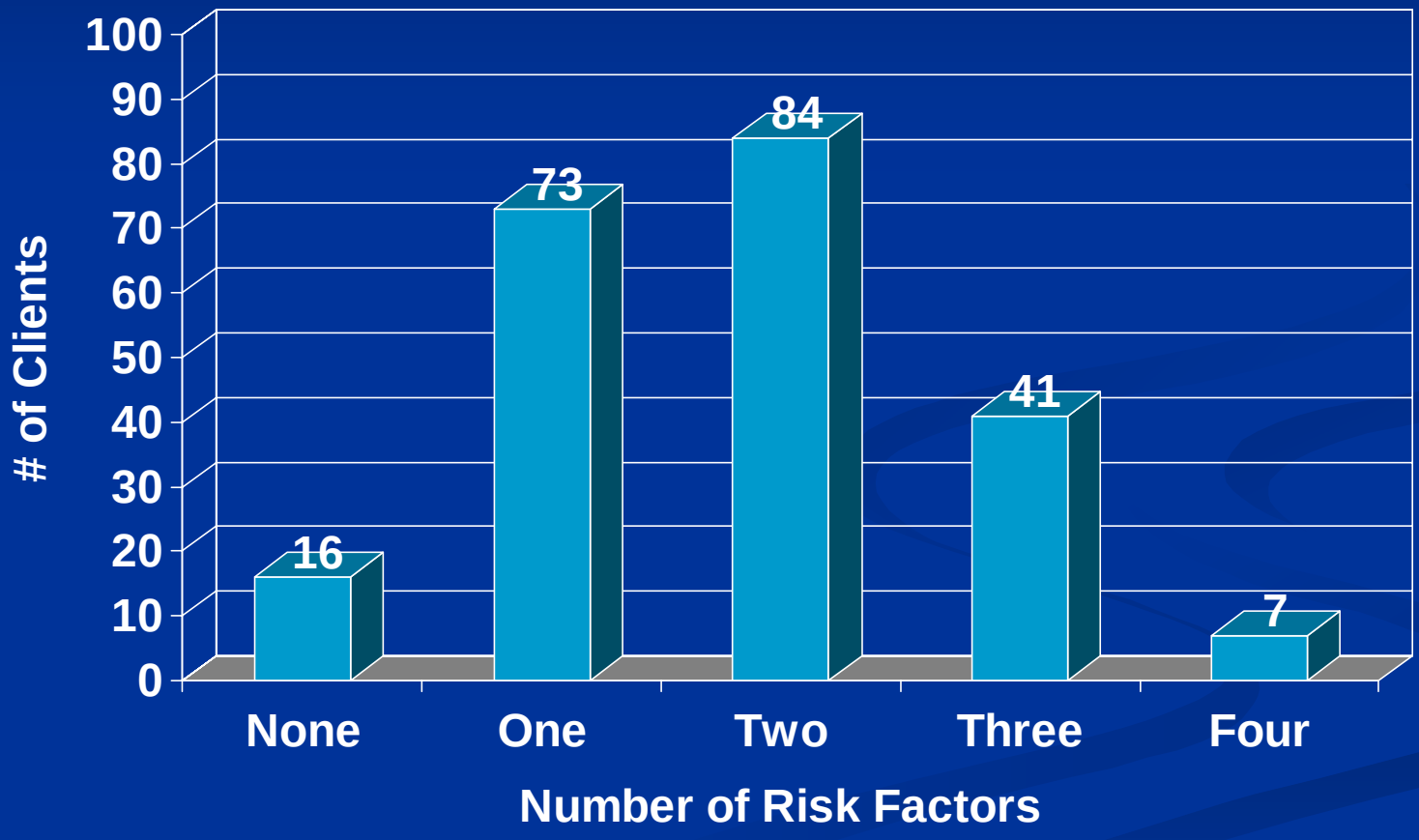
HMHS: Body Mass Index (BMI) from Vital Exam:



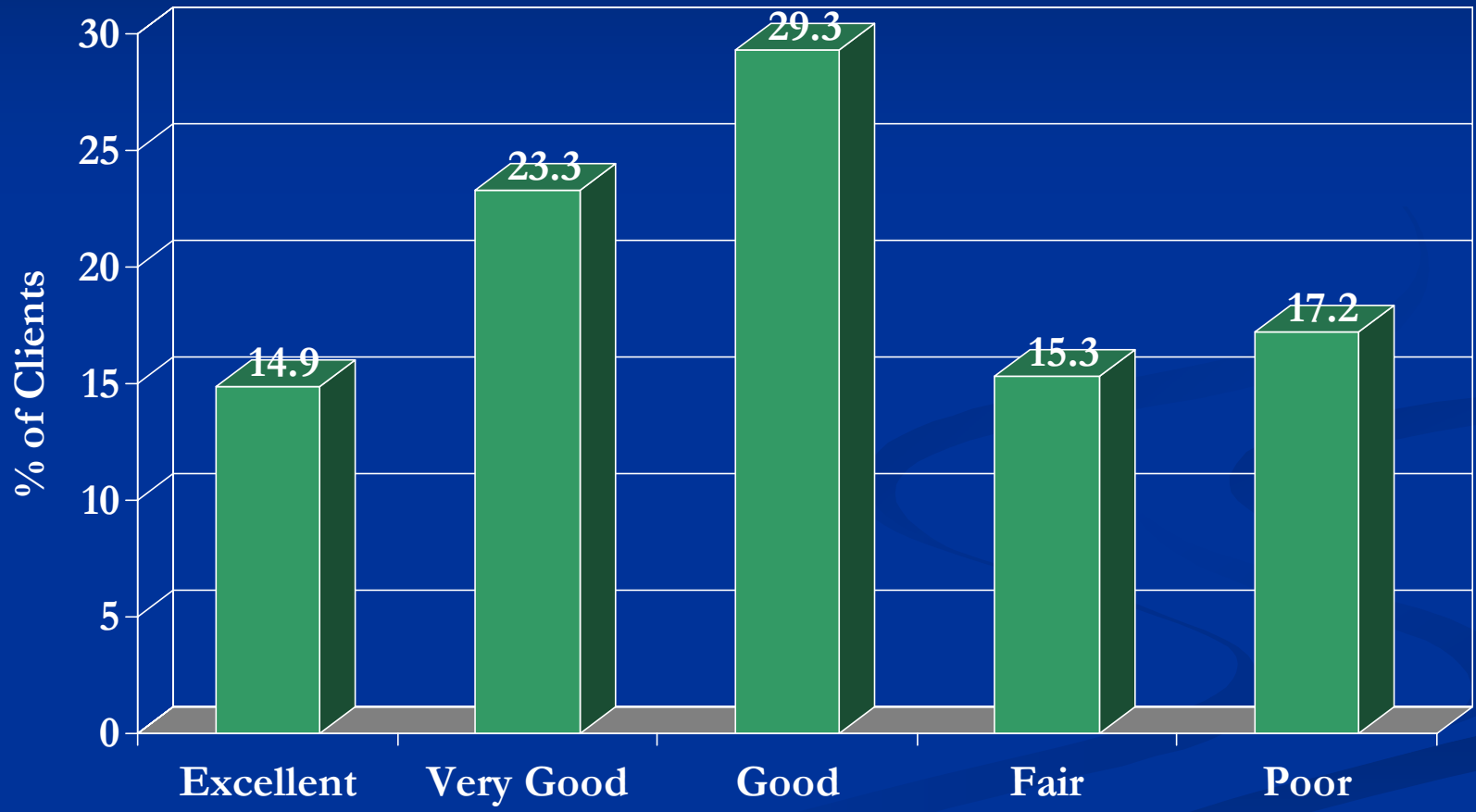
Mean=29.8 (sd=6.7), Median=29.1, Range from 14.4 to 49.9

BMI Categories: Underweight<18.5; Normal=18.5-24.9; Overweight=25-29.9; Obese≥30

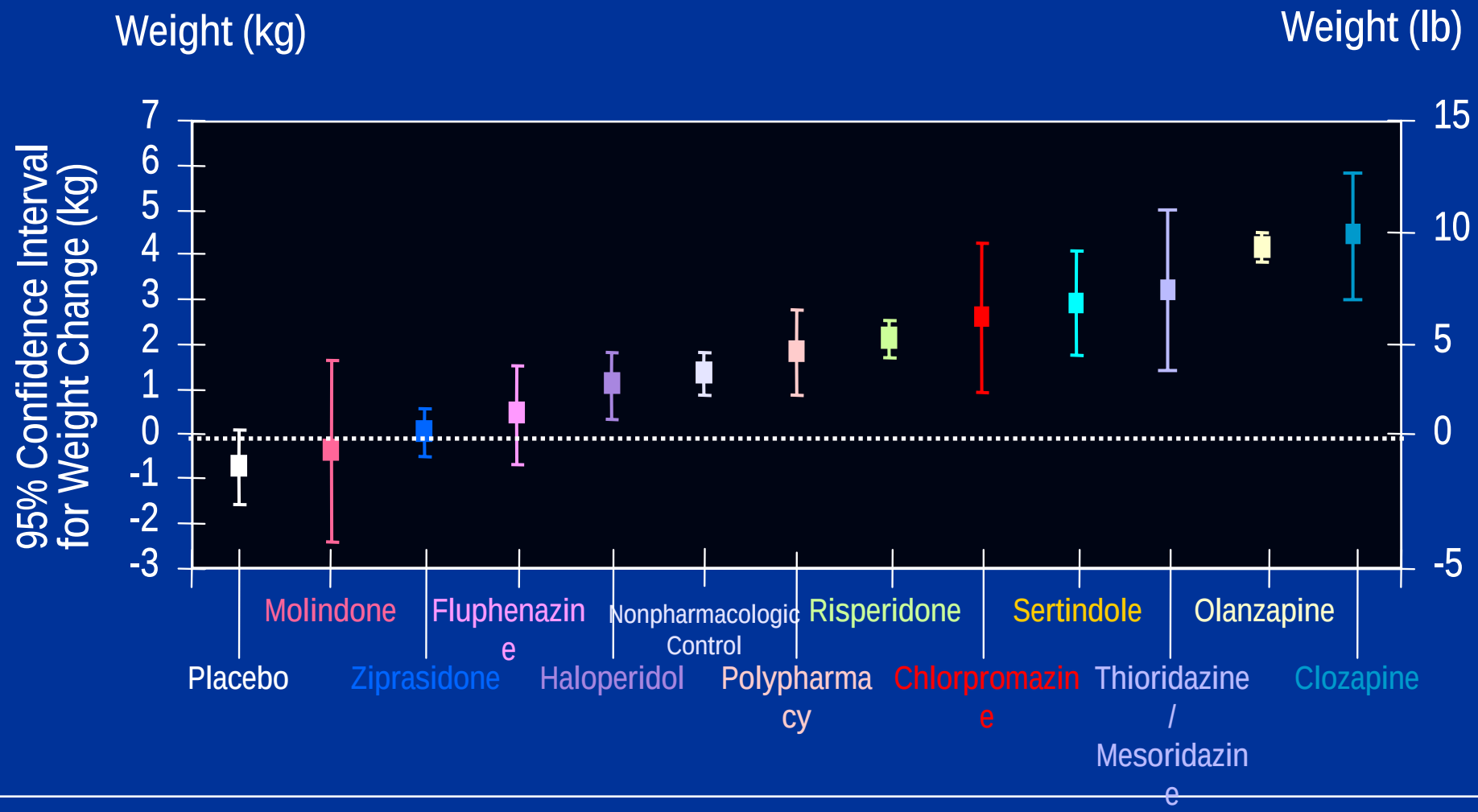
Risk Index – Number of factors from 4 possible – Diabetes, HTN, Overweight or Obese, and Smoking
Harborview MHC N=221



HMHS Nurse Assessed Compliance History of Medical Follow Through

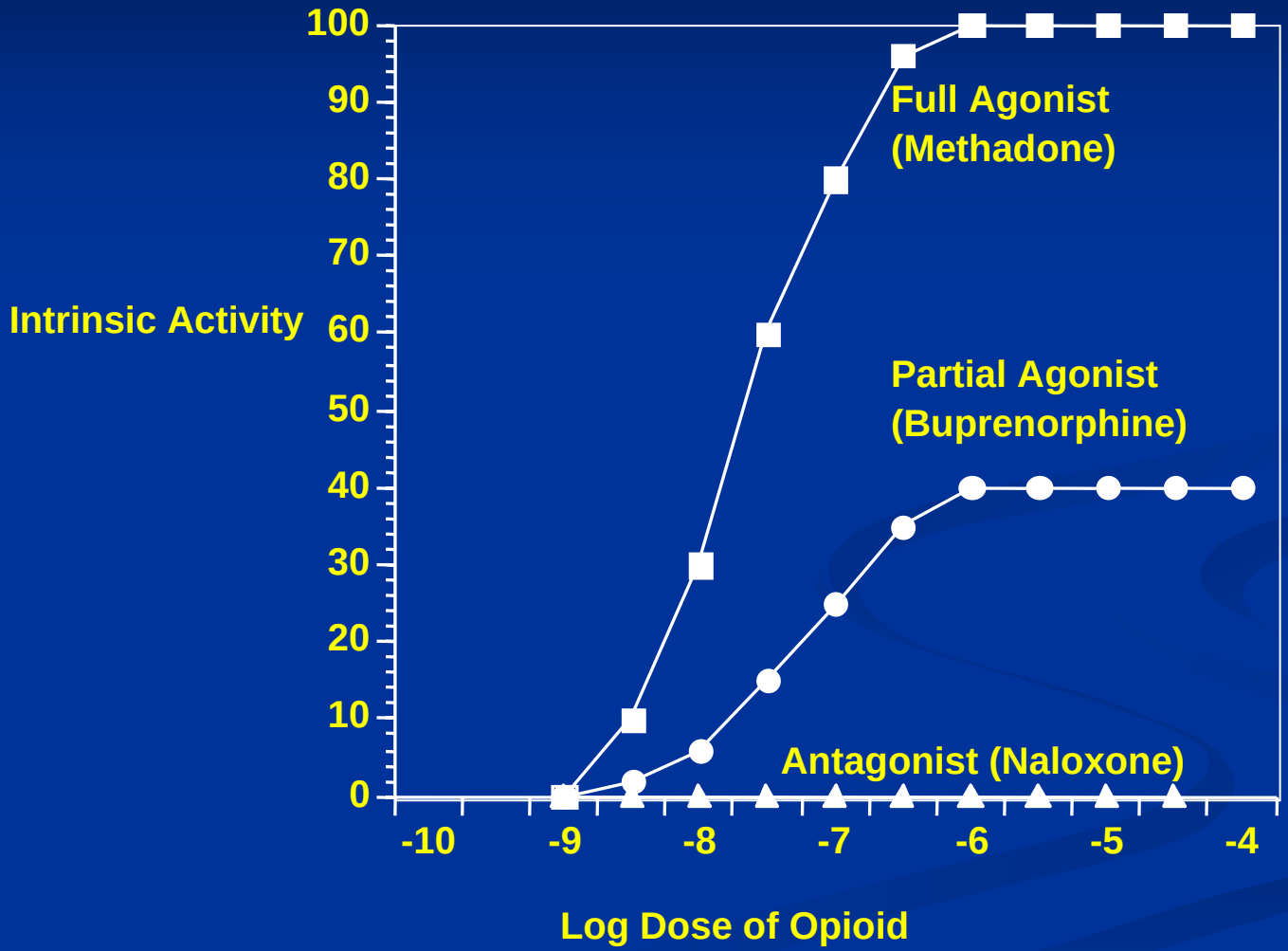


Meta-Analysis of Antipsychotic Agent-Related Weight Gain Estimated from a Random Effects Model After 10 Weeks



Allison et al. *Am J Psychiatry.* 1999;156:1686-1696.

Intrinsic Activity: Full Agonist (Methadone), Partial Agonist (Buprenorphine), Antagonist (Naloxone)



Stop the polypharmacy, I want to get off…..

Simplifying meds ….is a **MAJOR** medical/psychiatric intervention, may save thousands/yr in medical and medication costs as a side effect.

Simplifying meds….can increase compliance and decrease chances of Major medical complications, like DM, Hypertension, stroke, MI etc….

Stop the Polypharmacy I want to get off……

- Drug/Alc intervention is a MAJOR psychiatric intervention and may allow for all of the below like:
  - Decreasing or simplifying meds
    - And the benefits to physical health outlined above
  - Decreased hospitalization, homelessness, jail etc
  - Improved Quality of Life

Keep It Simple Stupid… MEDICATION STRATEGIES

- First verify Diagnosis….are the meds appropriate to the current Diagnosis
- Can meds be trimmed….for example meds added for an acute event may no longer be necessary……are additional meds REALLY needed for those on ATYPICALS
- Especially if on Clozaril or Olanzapine, delete other meds or use ones which don't cause weight gain etc

Meds and Metabolics

- 14 week trial, N= 101 , clozapine vs olanzapine vs riperidone vs haldol
- Results: **BIG** differences found for metabolics…
  - Increased glucose: clozapine, olanzapine, and haldol
  - Increased cholesterol: clozapine and olanzapine
- Results: **SMALL** differences found for mental symptoms:
  - clozapine> olanzapine> risperidone > haldol

    - Lindenmayer, Volavka et al Am J Psych 2002, 2003

Meds and Metabolics

- Retrospective chart review of 215 pts x 2.5 years comparing effects of : clozapine, olanzapine, risperidone, quetiapine, haldol, and fluphenazine….
- Results:
  - Glucose increased by clozapine, olanzapine and haldol
  - Triglyceride levels increased in clozapine and olanzapine
  - No changes associated with risperidone

    - Wirshing DA: J Clin Psych 2002……same results in large VA study

What about newer agents?

- Ziprasidone: studies consistently show wt, glucose, lipid neutral. IM clinical effect is solid and predictable. PO effect variable and hard to predict….may need higher doses…may work better for neg Sx

- Aripiprazole: appears to be wt, glucose, and lipid neutral. Early clinical experience suggest response profile more like Ziprasidone.

J Clin Psychiatry 2001 May;62(5):347-9

The apparent effects of ziprasidone on plasma lipids and glucose.

Kingsbury SJ, Fayek M, Trufasiu D, Zada J, Simpson GM.

Department of Psychiatry and the Behavioral Sciences, Keck School of Medicine, University of Southern California, Los Angeles 90033, USA.

METHOD: As part of a multicenter study examining different strategies for switching to ziprasidone from other antipsychotics, we evaluated weight and serum glucose, cholesterol, and triglyceride measurements at baseline and following 6 weeks on ziprasidone treatment in 37 patients at our site.

RESULTS: Short-term treatment with ziprasidone appeared to lead to

1. **significant reduction in serum cholesterol ($p < .001$) and**
2. **triglyceride levels ($p = .018$) independent of changes in BMI.**

3. **Ziprasidone treatment appeared to have no significant effect on BMI or glucose level, perhaps due to the small number of subjects.**
4. **CONCLUSION: Ziprasidone appears to independently lead to a lowering of serum lipid levels.**

Mechanism for Weight/DM

- Insulin hyper-secretion/resistance
  - Melkerson, Psychopharm Bull 03
  - Melkerson, J Clin Psych 2000
  - Hedenmalm, Drug Safety 2002
- Leptin
  - Atmaca, J Clin Psych 2003

Ratings: 10= best…WSH 10-07-03

survey of state hospital attendings

	Efficacy	Safety	Tolerability	Cost	Total
Clozaril	9	3	4	3	19
Risperidone	9	7	6	9	31
Olanzapine	9	5	8	3	25
Quetiapine	5	7	7	3	22
Ziprasidone	5	6	5	8	24
Aripiprazole	5	8	7	2	22

Atypicals and Health issues

Drug	Weight gain	Risk for diabetes	Worsening lipid profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	D	D
Quetiapine	++	D	D
Aripiprazole*	+/-	-	-
Ziprasidone*	+/-	-	-

+ = increase effect; - = no effect; D = discrepant results.

*Newer drugs with limited long-term data.

Source: *Diabetes Care*, February 2004

Olanzapine/Clozaril:
SLIMMING THE MEDS

- Manage UNNECESSARY Polypharmacy by TAPER and DELETION
- Replace DEPAKOTE with Lamictal, TOPOMAX or possibly Zonisamide
- Replace Remeron with an SSRI or Welbutrin etc

Weight/Lipid/DM strategies

- Add afternoon and eve **H2 blockers** like Ranitidine. (interview around when hunger and snacking is worst)

- Negotiate “DOS” (Drop One Snack) per day, as you are SLIMMING THE MEDS……esp carbohydrates like chips, fries, cookies…..fats and protein are better…INSULIN NONRESPONSE

WEIGHT/LIPID/DM STATEGIES

- Negotiate AOB (Add One Block) increase in WALKING per week or month depending on how inactive the person has been
- Eventual goal is 30 minutes of brisk (makes you breathe heavily) walking/day….use this time for positive goal setting too

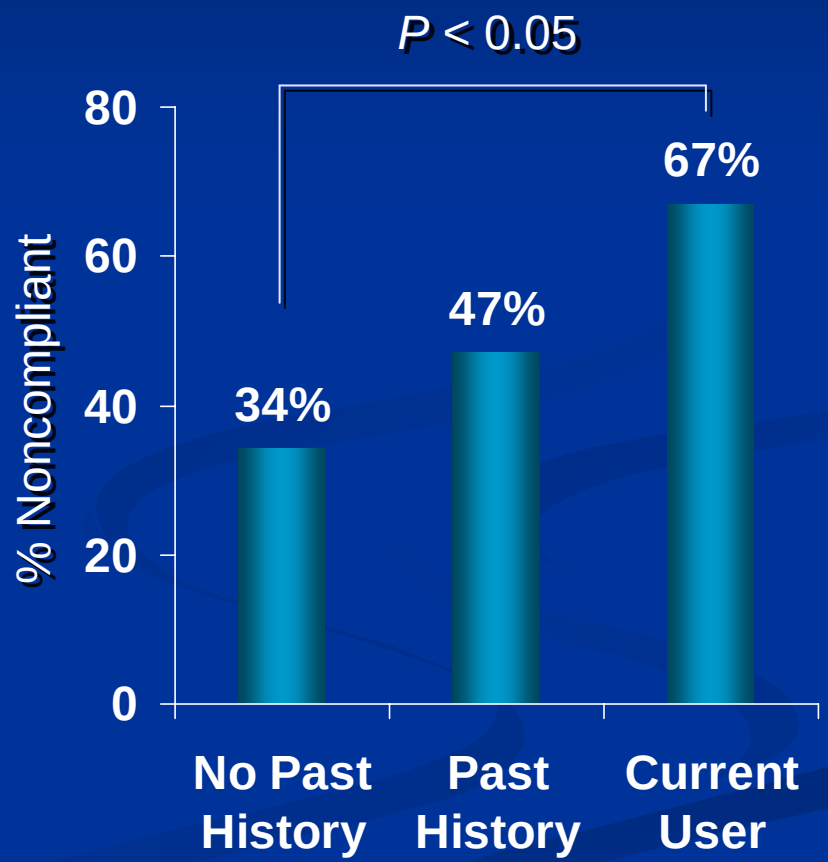
- Make sure the person has good shoes and a raincoat and does this rain or shine

WEIGHT/LIPID/DM STRATEGIES

- MEASURE CHANGES……WEIGHT Q MONTH IN PROGRESS notes
  - make this part of standard practice for nurses/doctors..
  - have a scale right by the MD nurse office
  - do Labs q 3-6 months as you are making changes
- Use MOTIVATIONAL FEEDBACK STRATEGIES with even small positive changes

Comorbid Substance Abuse Associated With Noncompliance in Schizophrenia

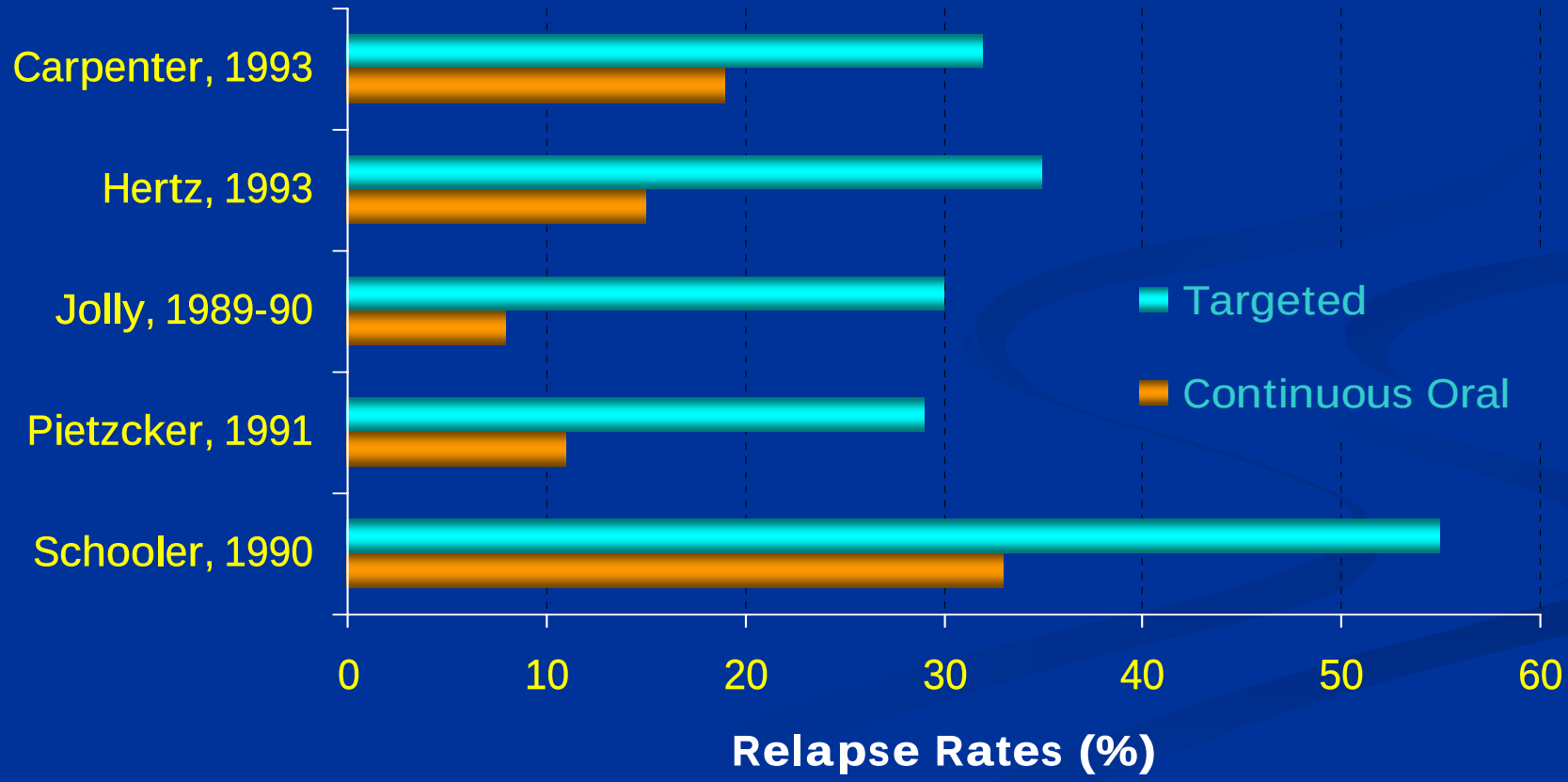
- Nearly half of all patients in a prospective 4-year study (N = 99) were active substance abusers (n = 42)
- Patients who actively abused substances were significantly more likely to be noncompliant



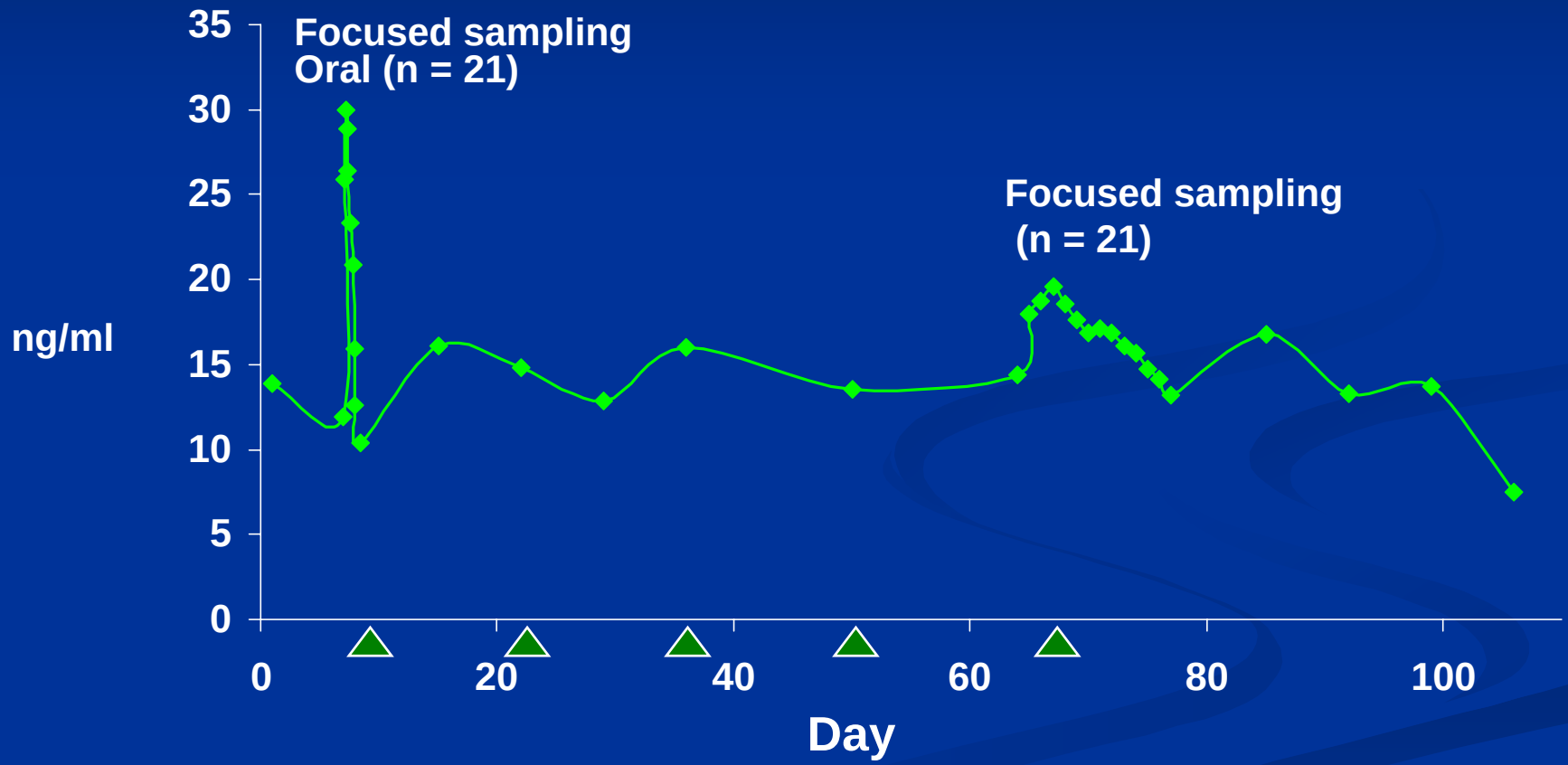
Hunt GE et al. *Schizophrenia Res*. 2002;54:253-264.

Relapse Rates Are Lower With Continuous Antipsychotic Therapy

One year relapse rates with continuous or targeted oral conventional antipsychotic maintenance therapy



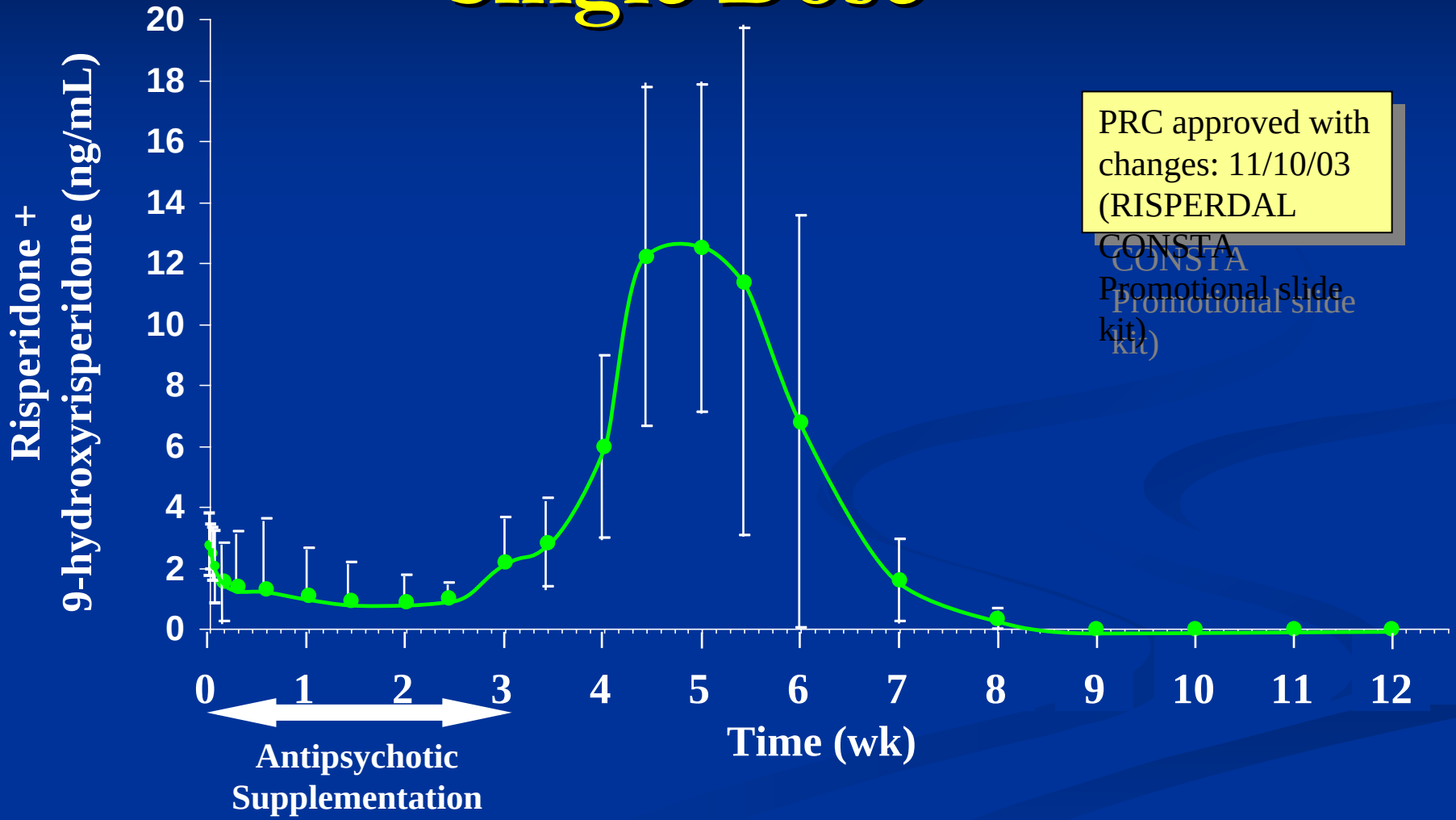
RISPERDAL CONSTA™: Mean Active Moiety Concentrations



*25-mg dose, every 2 weeks.

Eerdekens M et al. Poster. 1999 ACNP Meeting; Acapulco, Mexico

Blood Levels Over Time After Single Dose*



PRC approved with changes: 11/10/03 (RISPERDAL CONSTA Promotional slide kit)

*25-mg dose, N = 14.

Data on file, Janssen Pharmaceutica Products, L.P.

ANTABUSE

2) Cause Negative Symptoms

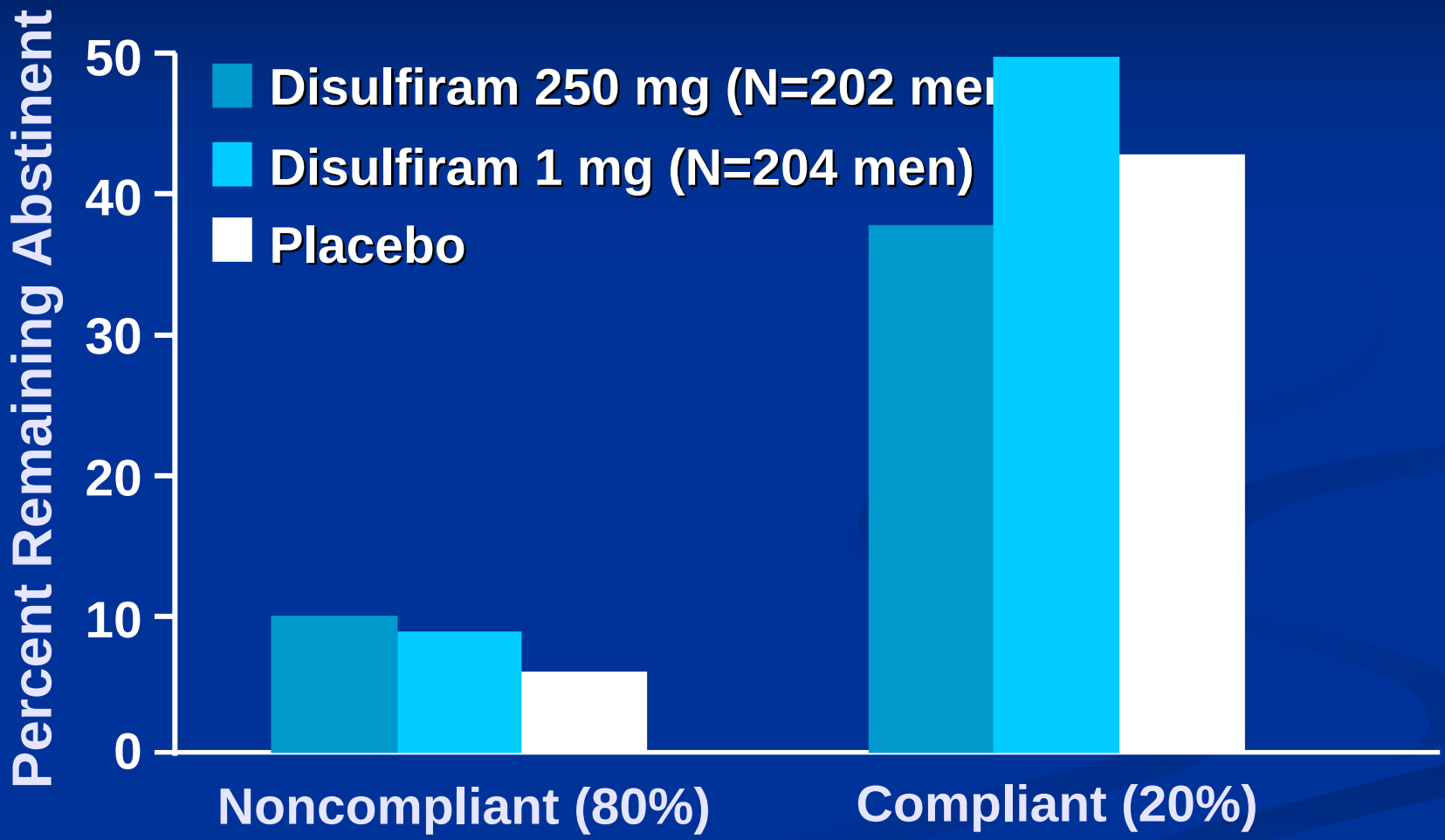
a) Alcohol

1. Antabuse (disulphram)

ADH ALDH

ETOH ←→ Acetaldehyde ←X→ Acetate

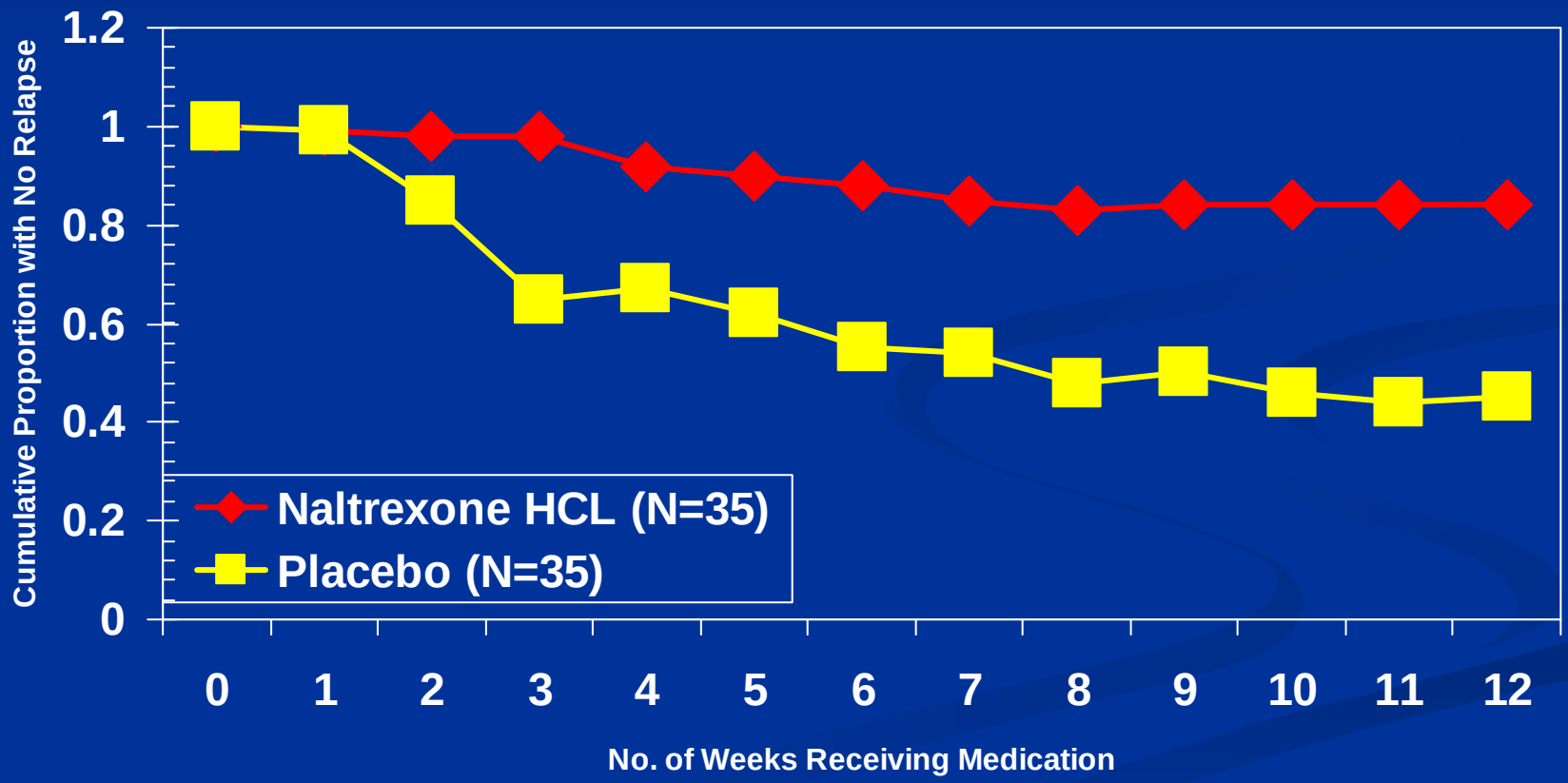
Disulfiram and Abstinence Rates



Fuller RK et al. JAMA. 1986(Sept);256(11):1449-1455

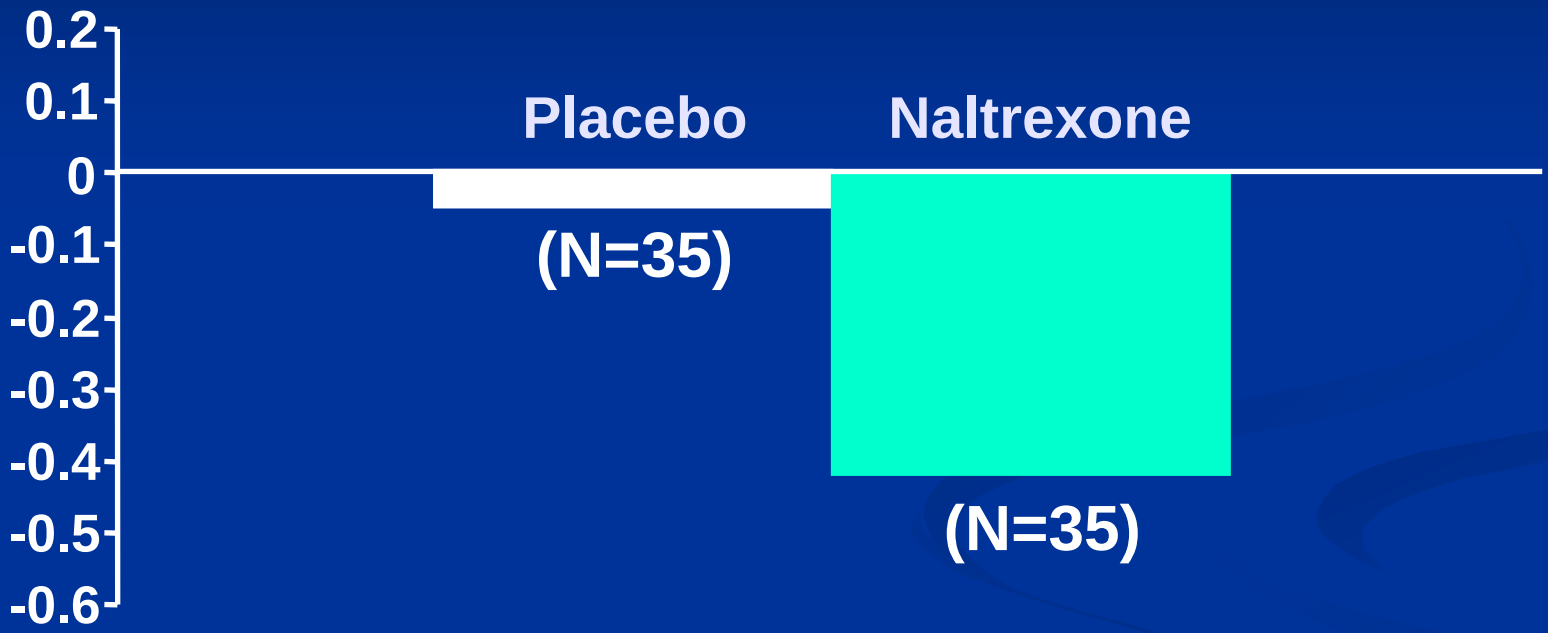
NALTREXONE IN THE TREATMENT OF ALCOHOL DEPENDENCE

Cumulative Relapse Rate



Volpicelli et al., 1992

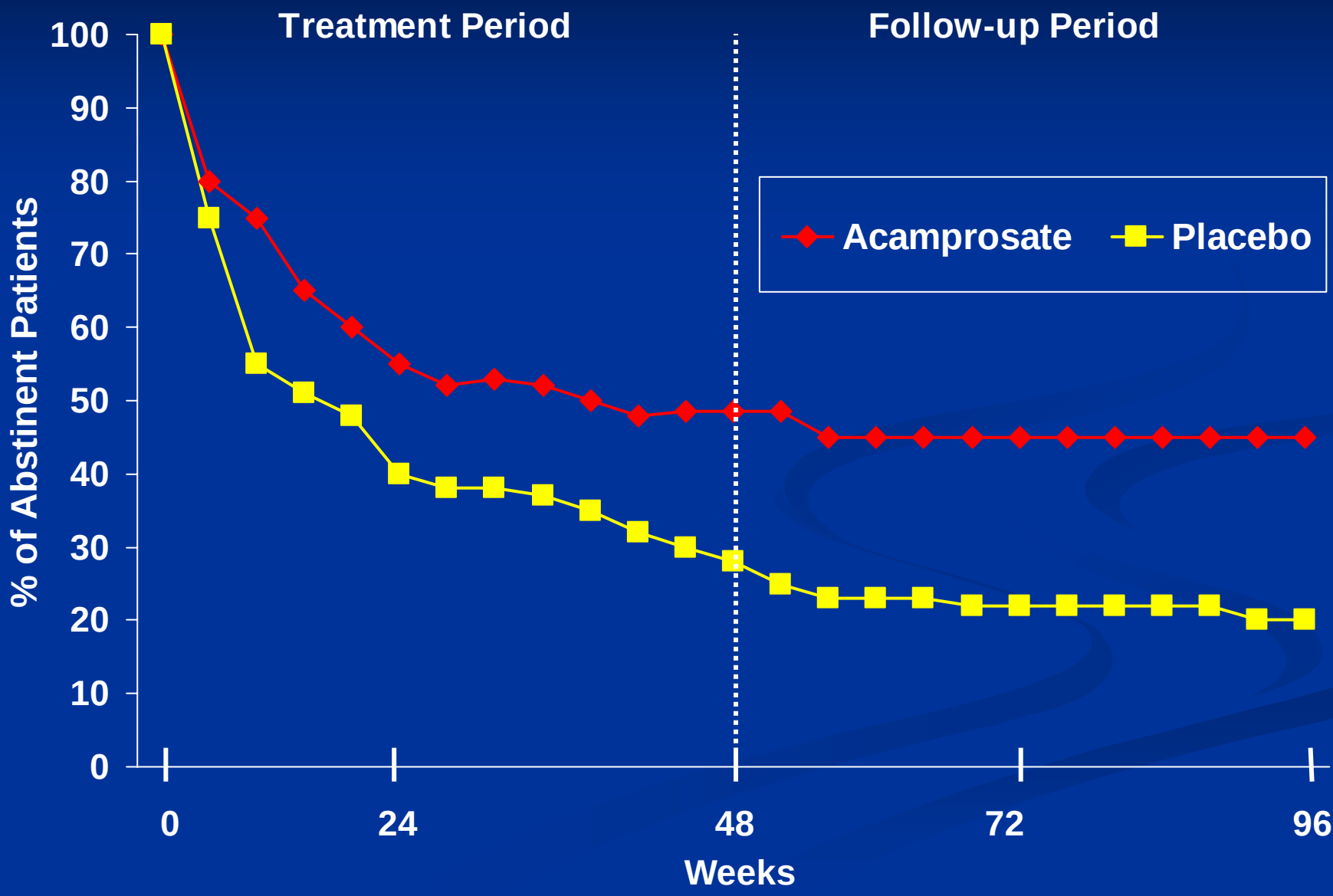
Subjective "High" Produced by Alcohol



+1 = Increased high
0 = No change in high
-1 = Decreased high

p<0.006; Volpicelli JR et al. Am J Psychiatry. 1995(April);152(4):613-615

ACAMPROSATE RELAPSE RATES



Acamprosate (N-acetylhomotaurine)

Current Status

- In 16 of 18 European/Asian clinical trials involving over 3,000 patients, acamprosate increased abstinence rates by about 50%
- Availability: currently approved in about 40 countries in Europe, Asia and the U.S.

Acamprosate (N-acetylhomotaurine)

- Mechanism: interacts with glutamate and GABA neurotransmitters systems (PI)
- In animal models of alcohol dependence, acamprosate reduced deprivation-induced drinking
- Does not cause dependence or withdrawal
- May reduce protracted withdrawal symptoms

Am J Addict 2002
Spring;11(2):141-50

The differential effects of medication on mood, sleep disturbance, and work ability in outpatient alcohol detoxification.

Malcolm R, Myrick H, Roberts J, Wang W, Anton RF.

A double-blind, randomized controlled trial of patients (n = 136) meeting DSM-IV criteria for alcohol withdrawal and stratified based on detoxification history were treated with **carbamazepine or lorazepam** for 5 days on a fixed dose tapering schedule. Mood symptoms improved for all subjects regardless of medication or detoxification history.

- **main effect favoring carbamazepine in reducing anxiety (p = 0.0007).**

- **main effect of medication on sleep that again favored carbamazepine (p = 0.0186).**

In this study of outpatients with mild to moderate alcohol withdrawal, carbamazepine was superior to lorazepam in reducing anxiety and improving sleep.

1: JAMA. 2004 Apr 21;291(15):1887-96.

Treatment of depression in patients with alcohol or other drug dependence: a meta-analysis.

Nunes EV, Levin FR.

DATA SYNTHESIS: For the HDS score, the pooled effect size from the random-effects model was 0.38 (95% confidence interval, 0.18-0.58). Heterogeneity of effect on HDS across studies was significant (P <.02), and studies with low placebo response showed larger effects.

Moderator analysis suggested that diagnostic methods and concurrent psychosocial interventions influenced outcome.

Studies with larger depression effect sizes (>0.5) demonstrated favorable effects of medication on measures of quantity of substance use, but rates of sustained abstinence were low.

CONCLUSIONS: **Antidepressant medication exerts a modest beneficial effect for patients with combined depressive- and substance-use disorders. It is not a stand-alone treatment, and concurrent therapy directly targeting the addiction is also indicated**.

12 step facilitation for psychiatrists and other MH clinicians

- Why?
  - 20-50% of psychiatric outpts will have current, history or episodic substance problems
  - Substance treatment may be unavailable or even if used, 12 step will likely be involved
  - Positive effects include not only the group support and socialization, but key psychological/therapeutic content elements.
  - 12 Step facilitation is AN **EVIDENCE BASED PRACTICE** with manual and extensive literature…..
  - how many of you have ever seen the manual?

Group Therapy

- Process group , or theme/didactic
- Structured/ unstructured
- Pt co-therapist
- Activities/celebrating birthdays etc
- Using a “check-in”
  - Name/ Addiction dx/sobriety date/what I’m doing to stay sober
  - Psych dx/meds/what I’m doing to get better

Groups: Check-In

- Using a “check-in”
  - Name
  - Addiction dx/sobriety date/what I’m doing to stay sober…Going to outside meetings???
  - Psych dx…Meds, Med compliance….what I’m doing to get better…work, activities
  - How am I feeling on a 10 pt scale
  - Relapse cues
  - Do I need time in group for a current problem

Medications: counselor's role

- Ask the pt about :
  - Compliance…
    - "sometimes people forget their medications…how often does this happen to you?" …ie % not taking
    - "Do you ever go days or weeks off your medications?"
      - How often, how long, why??
  - Effectiveness…
    - "how well do you think the meds are working?…
    - what do you notice…
    - here is what I notice…..
  - Side Effects….
    - " are you having any side effects to the medication?…
    - what are they…
    - have you told the prescriber?
    - do you need help with talking to the presciber?

It may not be that the med(s) stopped working, but……

- The patient stopped the med
- The patient stopped the med AND used drugs and/or alcohol……
- OR lowered the med and used…
- OR used on top of the med….
- Stimulants (cocaine/amphets) are most MSE destructive.

A NEW/OLD APPROACH

- Stop the polypharmacy, I want to get off…….fewer meds = better compliance and less cost
- Decreasing the chance of Major medical complications, like DM, Hypertension, stroke, MI etc…..is a MAJOR medical/psychiatric intervention
- Consider dangerous iatrogenic causes…"do no harm", AS WELL AS increase EXERCISE, DIET ETC
- Re-thinking the role of IM meds, now that Consta is coming, is VERY important

Stop the Polypharmacy I want to get off……

- Drug/Alc intervention is a MAJOR psychiatric intervention and may allow for all of the below like:
  - Decreasing or simplifying meds
    - And the benefits to physical health outlined above
  - Decreased hospitalization, homelessness, jail etc
  - Improved Quality of Life

And just remember what Fred says:

Stay Cool and Keep Calm…..